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**Labs Say They Have Nearly All the Tools to Make Artificial Life**

*By Ronald Kotulak*

*Chicago Tribune (KRT)*

     CHICAGO--More than 3.5 billion years after nature transformed nonliving matter into living things, populating Earth with a cornucopia of animals and plants, scientists say they are finally ready to try their hand at creating life.

     If they succeed, humanity will enter a new age of "living technology" where harnessing the power of life to spontaneously adapt to complex situations could solve problems that currently defy modern engineering abilities.

     Scientists eagerly talk of a new world of ultrasmall living machines where marvelously made-to-order cells heal the body, clean up pollutants, send computing into the stratosphere, transform electronics and communication, make materials self-repairing and much more.

     The researchers say it may be possible to make sweaters that mend themselves. Or computers that fix their own glitches.

     While some experts see this new technology as providing unlimited benefits, others worry about the moral appropriateness of man-made life and the introduction of new species with the potential to evolve into creatures that could run amok.

     "It's certainly true that we are tinkering with something very powerful here," said artificial life researcher Steen Rasmussen of Los Alamos National Laboratory.

     "But there's no difference between what we do here and what humans have always done when we invented fire, transistors and ways to split the atom," he said. "The more powerful technology you unleash the more careful you have to be."

     Such concern is escalating as more than 100 laboratories study processes involved in the creation of life, and scientists say for the first time that they have just about all the pieces they need to begin making inanimate chemicals come alive.

     Unlike any other technology invented by humans, creating artificial life will be as jarring to our concepts of ourselves as discovering living creatures on other planets in the universe. It would also bring into sharper focus the age-old questions of "What is life?" and "Where do we come from?"

     "The ability to make new forms of life from scratch--molecular living systems from chemicals we get from a chemical supply store--is going to have a profound impact on society, much of it positive, but some of it potentially negative," said Mark Bedau, professor of philosophy and humanities at Reed College, Portland, Oregon, and editor-in-chief of the Artificial Life Journal.

     "Aside from the vast scientific insights that will come, there will be vast commercial and economic benefits, so much so that it's hard to contemplate in concrete detail what many of them will be," he said.

     But the first artificial life is also likely to shock people's religious and cultural belief systems.

     "People from many different backgrounds have special views about what life is: how it originates; the special sanctity it has; the special dignity it deserves," Bedau said. "The ability to make new forms of life will perturb all of that. We need to think through the implications and how we are going to react to them."

     Yet so doable does artificial life now seem that the number of U.S. labs working in the field jumped from about 10 four decades ago to more than 100 today.

     Spearheading the drive is the European Union's Programmable Artificial **Cell** Evolution (PACE) project recently established with a grant of about $9 million. PACE is scheduled to open the first institution devoted to creating artificial life, called the European Center for Living Technology, in Venice, Italy, in April, staffed by European and U.S. researchers.

     "It's a synthetic **biology** revolution," said John McCaskill, professor of theoretical biochemistry at Friedrich Schiller University, Jena, Germany, who is overseeing the European Union's artificial life program.

     "We obviously don't want to be too polemic about how rapidly this is going to transform society," he said. "But I think that we are seeing a new feature of science and technology where systems are autonomously adaptive and that this is a significant component of the design process."

     Scientists are trying to unravel the grand mystery of how life originated on Earth, and possibly Mars and other places in the universe. How is it that when atoms of carbon, oxygen, hydrogen and nitrogen are organized in the right way, for example, they make a carrot. Arranging a whole bunch more atoms in a different way produces a human being.

     Life is generally not thought of as being mechanical. But a **cell** basically is a miniature machine in which nonliving atoms are constantly being rearranged to make the moving parts that imbue it with life.

     The **cell**, the basic unit of all living things, becomes much more than all of its parts. New properties emerge that give a **cell** the power to repair itself, reproduce and adapt to changing environments.

     A key element of all living systems is the ability to evolve through natural selection. Things that are successful survive while those that fail to adapt die off. The idea is to incorporate this evolutionary design process into technology that people can use, making things that are complicated and well adapted without having to figure out in advance all the problems that could arise.

     "Our technology right now is facing a complexity crisis. We need to make things that are more complicated if we want to have new kinds of functionality," Bedau said. "We want to have better telephone switching networks, better computers, better spacecraft but we don't know how to do it."

     "If we could make life we would have a new insight into how to make things more complicated," he said. "We could apply these principles in other areas. Life is very, very complicated but it also repairs itself, it organizes itself and it adapts spontaneously to changes. It would be nice to have a space shuttle that can do those things or a telephone switching network that can grow and adapt in an organic way."

     It is a dream long pursued by scientists who now believe that it may be possible to create the first artificial unit of life in the next 5 to 10 years.

     "We've been saying that for the last 50 years," said David W. Deamer, professor of biomolecular engineering, University of California, Santa Cruz, a pioneer in the field. "What makes it different now is that we have a critical mass of people interested in the field and some recent breakthrough discoveries."

     From Deamer's point of view, the risk that artificially created life could get out of hand is "infinitesimally small."

     "There's nothing we could make that could compete with the predators that are out there and have had 3 billion years to evolve," he said. "Bacteria eat anything. They eat jet fuel, oil deposits, chlorinated hydrocarbons, anything. They will eat anything that we put out there to compete with them."

     Another safeguard scientists are designing to provide total control over artificial cells is to make their lives dependent on chemicals that do not exist in the environment. Withdrawing the critical chemicals would result in the death of the cells, particularly if they should escape into the environment.

     What makes life possible, scientists believe, is the natural tendency of atoms to self assemble into molecules and for molecules to assemble into increasingly complicated structures.

     All of the basic elements of life--the amino acids that make proteins and the nucleotides that make DNA and its sidekick RNA--have been produced in the laboratory from chemicals thought to have been present on the primitive earth: hydrogen, methane, ammonia, formaldehyde, cyanide, thiols and hydrosulfide.

     Some of these elements are so easy to self assemble that amino acids are found on meteorites originating at the beginning of the solar system. The Murchinson meteorite, for example, contains a wide variety of chemicals, including simple amino acids and fats called lipids. When put in water lipids spontaneously form bubble-shaped membranes that resemble cells.

     Earth coalesced 4.5 million years ago during the formation of the solar system, and was too hot for life for several hundred thousand years. But it didn't take long after the Earth cooled for life to appear. Scientists estimate that fossils of primitive organisms appeared 3.8 billion years ago.

     Researchers argue over the definition of life, but there is general agreement that it has to have three things: a container, such as the membrane wall of a **cell**; metabolism, the ability to convert basic nutrients into a cell's working parts; and genes, chemical instructions for building a **cell** that can be passed on to progeny and change as conditions change.

     Each of these critical elements have now been made in the laboratory, albeit in rudimentary form, and scientists say for they are ready to try to put them all together in one working unit.

     "We have quite a bit of knowledge about how these different systems work independently," said microbiologist Martin Hanczyc of Massachusetts General Hospital. "We are at a point where we can start taking these things into the laboratory and do experiments."

     "Whether we'll be able to synthesize a living **cell** in the near future is a big question. But we can start exploring that possibility with what we have available now," said Hanczyc, who along with Harvard's Jack Szostak, is able to make artificial cellular membranes grow and divide.

     One of the tricks they learned is how to use the remarkable properties of clay, which is thought to have been abundant on the early earth. Clay has natural catalytic properties--it speeds up the assembly of lipid membranes 100-fold, for example, and also hastens the assembly of genetic material called ribonucleic acid (RNA). RNA can be made in the laboratory from raw chemicals.

     Their findings indicate that critical chemicals essential for life--membranes and genes--can spontaneously be brought together and they have succeeded in creating **cell**-like containers that have incorporated laboratory-made RNA.

     How the first genes got together is a big mystery. Many scientists believe that RNA may have preceded DNA because it can both carry genetic instructions and make copies of itself. Today DNA serves to preserve the chemical instructions for making and maintaining an organism, while RNA mostly translates those instructions into proteins. DNA and RNA are nearly identical in structure.

     David Bartel of the Whitehead Institute for Biomedical Research is trying to make RNA from raw chemicals and so far he has succeeded in getting compounds to assemble into small RNA sequences that can make partial copies of themselves.

     Bartel calls it test tube evolution. More than 1,000 trillion random RNAs are squirted into a test tube and allowed to self-assemble into millions of different sequences. A few of those sequences acquired the ability to make copies of RNA sequences, a fledgling step towards artificial life that can reproduce itself and evolve.

     Rasmussen of Los Alamos National Laboratory and Liaohai Chen of Argonne National Laboratory believe they have a good chance of making an artificial **cell** by using a slightly different version of DNA called polypeptide nucleic acid (PNA).

     Unlimited variations of PNA can easily be made. They love to stick to the surface of membranes where they can suck up nutrients and hopefully churn out all kinds of novel chemicals including more **cell** membrane lipids.

     "We have all the pieces, and we have demonstrated that our metabolism can produce the container molecules," Chen said. The protocells that assemble are 10 million times smaller than a bacterium, he said.

     The idea is to get all the parts working together so that the artificial cells would not only make daughter cells but would also be able to manufacture custom-made chemicals now beyond the reach of engineers, such as self repairing materials.

     "Once we have self-reproducing entities that can be programmed, you can do all kinds of useful things," Rasmussen said. "You don't need to build the useful molecules, you can actually have them self-reproduce, you can grow them."

     Physicist Norman Packard, who established the first company, ProtoLife, to capitalize on the new field of living technology, thinks of artificial cells as tiny machines that can be programmed to clean out arteries, deliver drugs to specific sites in the body and perform other jobs with great precision.

     "The goal of the company is to realize the vision of producing living artificial cells, and also producing other forms of living chemistry, and then programming them to do useful chemical applications," he said. "The range of useful chemical functions we ultimately envision is vast."